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- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: COMBINATIONS OF ANTISENSE OLIGONUCLEOTIDES DIRECTED AGAINST THYMIDYLATE SYNYTHASE MRNA AND USES THEREOF

(57) Abstract: Effective combinations of antisense oligonucleotides directed against thymidylate synthase mRNA are provided for use in cancer therapies. Combinations of antisense oligonucleotides have enhanced activity compared to the activity of the individual antisense oligonucleotides when used alone. The combinations may be used in conjunction with one or more chemotherapeutic agents to enhance the effects of the chemotherapeutic(s). Such antisense oligonucleotide combinations constitute improved antisense therapies with application to a variety of cancers or proliferative disorders, including drug resistant cancers.

INTERNATIONAL SEARCH REPORT



Intermediation No PCT/CA 20480

A. CLA	ASSIFIC	ATION OF	SUBJECT	MATTER ,	
IPC	7	A61K31	./70	C12N15/	11

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols) $IPC\ 7\ C12N$

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BIOSIS, EPO-Internal, SEQUENCE SEARCH, MEDLINE, EMBASE

Category Citation of document, with Indication, where appropriate, of the relevant passages	Relevant to claim No.
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X Further documents are listed in the continuation of box C.	Patent family members are listed in annex.		
 Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed 	 "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family 		
Date of the actual completion of the international search	Date of mailing of the International search report		
8 August 2003	21/08/2003		
Name and mailing address of the ISA	Authorized officer		
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Morawetz, R		

INTERNATIONAL SEARCH REPORT

Internal Application No PCT/CA 30480

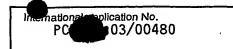
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X BERG RANDAL W ET AL: "A 'combination antisense' oligonucleotide strategy to downregulate thymidylate synthase: Two oligos are better than one." PROCEEDINGS OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH ANNUAL, vol. 43, March 2002 (2002-03), page 577 XP001154122 93rd Annual Meeting of the American Association for Cancer Research; San Francisco, California, USA; April 06-10, 2002, March, 2002 ISSN: 0197-016X Y the whole document Y FERGUSON PETER J ET AL: "Antisense down-regulation of thymidylate synthase to suppress growth and enhance cytotoxicity of 5-FUdR, 5-FU and Tomudex in HeLa cells." BRITISH JOURNAL OF PHARMACOLOGY,	1,4-9, 12-14
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INTERNATIONAL SECH REPORT

Internal Application No
PCT/CA 0480

0.60	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	101/07		
Category °		Relevant to claim No.		
Category	Citation of document, with indication, where appropriate, or the research			
Y	WO 99 15648 A (KOROPATNICK DONALD JAMES; VINCENT MARK DAVID (CA); ZENECA LTD (GB)) 1 April 1999 (1999-04-01) the whole document	1–15		
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Box I	Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This inte	ernational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. X	Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
	Although claims 7-11 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2.	Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful international Search can be carried out, specifically:
3.	Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II	Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This Inte	ernational Searching Authority found multiple inventions in this international application, as follows:
1.	As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.	As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.	As only some of the required additional search fees were timely paid by the applicant, this international Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.	No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remari	The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT



Intel Conal Application No
PCT/CA 03,00480

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